

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1-23 (Cancelled).

24. (Cancel).

25. (Currently Amended) A The conjugate as claimed in claim 24 29 wherein the bioreductive moiety is non-cytotoxic.

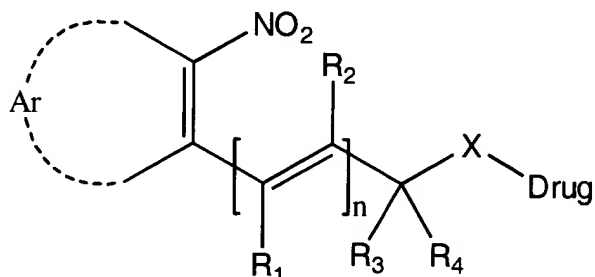
26-28 (Cancel).

29. (Currently Amended) ~~A conjugate as claimed in claim 28 which A~~
bioreductive conjugate comprising a bioreductive moiety with at least one therapeutic agent linked thereto and physiologically acceptable derivatives thereof wherein the bioreductive moiety incorporates an aromatic ring substituted with a nitro group and the conjugate is such that bioreduction of the nitro group causes release of the therapeutic agent by a through bond elimination and the residue of the bioreductive moiety to undergo an intramolecular cyclization reaction in which the nitrogen of the original nitro group provides an atom of the thus formed ring.

RECEIVED
DEC 30 2003
TECH CENTER 1600/2900

wherein the therapeutic agent to be released on bio-reduction is bonded to the aromatic ring via a side chain incorporating one or more double bonds which are located in the side chain between said therapeutic agent and the aromatic ring, which is/are conjugated to the aromatic ring, and which is/are displaceable to provide for elimination of said therapeutic agent moiety and formation of an arrangement of double bonds such that the residue of the bio-reductive moiety is capable of undergoing the intramolecular cyclisation reaction, and

wherein said conjugate is of the general formula (I)



in which

the dashed lines represent completion of a substituted or unsubstituted aromatic ring system;

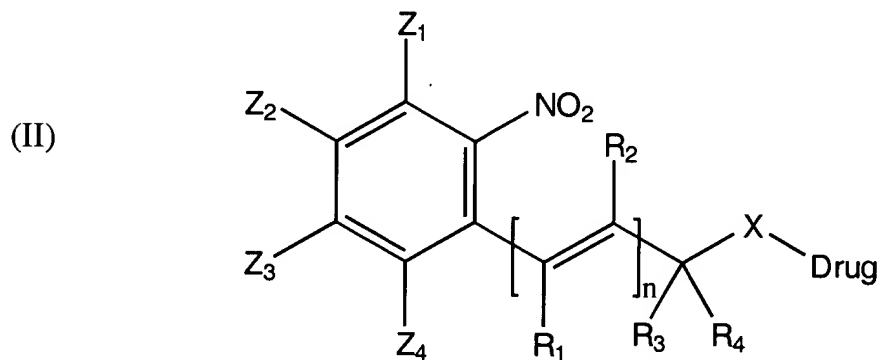
Drug is a therapeutic agent;

X is a linker (which may be part of the drug) and ~~is may for example be O, -NH, S, an amide, alcohol, phenol, carboxylic acid (carboxylate), carbonate, phosphate, sulphate or sulphonate;~~

R_1 , R_2 , and R_3 ~~and~~ R_4 are independently hydrogen, and R_4 is a substituted or unsubstituted alkyl, ~~aryl, halide, amine, alkoxy, ether, ester, alcohol, phenol, nitro, amide, thiol, sulphate, phosphate, or phosphonate;~~ and

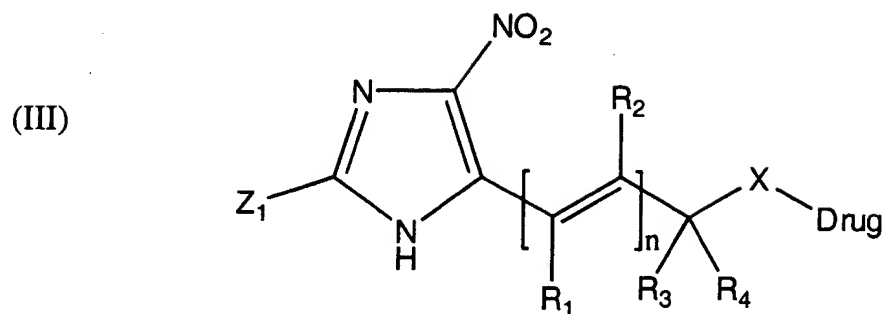
n is 1 to 3.

30. (Currently Amended) A The conjugate as claimed in claim 29 ~~which~~ wherein said conjugate is of the general formula (II)



wherein Z , Z_2 , Z_3 and Z_4 are independently hydrogen, substituted or unsubstituted alkyl, aryl, halide, amine, alkoxy, ether, ester, alcohol, phenol, nitro, amide, thiol, sulphate, phosphate, or phosphonate.

31. (Currently Amended) A The conjugate as claimed in claim 29 ~~which~~ wherein said conjugate is of the general formula (III)



32. (Currently Amended) A The conjugate as claimed in claim 29 wherein $n=1$.

33-36 (Cancel).

37. (Currently Amended) A The conjugate as claimed in claim ~~24~~ 29 wherein the therapeutic agent is an anti-infective, analgesic, anaesthetic, anti-inflammatory or anti-neoplastic agent.

38. (Currently Amended) A therapeutic composition comprising a ~~bio-reductive~~ the conjugate as claimed in claim ~~24~~ 29 in conjunction with a therapeutically acceptable carrier.

39. (Cancelled).

40. (Currently Amended) A method of therapeutic treatment, wherein the therapeutic treatment is for the treatment of a condition associated with hypoxia and/or ischemia, comprising administering to a subject in need of thereof a therapeutically effective amount of a bioreductive conjugate as claimed in claim ~~24~~ 29.

41. (Currently Amended) A method of therapeutic treatment, wherein the therapeutic treatment is for the treatment of an inflammatory condition, diabetes, atherosclerosis, stroke, sepsis, Alzheimer's disease and other neurological diseases, cancer, kidney disease, digestive diseases, liver disease, chronic periodontitis and ischemia following tissue transplantation, comprising administering to a subject in need of thereof a therapeutically effective amount of a bioreductive conjugate as claimed in claim ~~24~~ 29.

42. (Previously Presented) The method as claimed in the claim 41 when the therapeutic treatment is for the treatment of rheumatoid arthritis or other arthritic condition.

43. (Previously Presented) The method as claimed in claim 41 wherein the therapeutic treatment is for the treatment of an inflammatory condition of soft tissue.

44. (Previously Presented) The method as claimed in claim 42 wherein the therapeutic treatment is for the treatment of a gastrointestinal disorder.

45. (Previously Presented) The method as claimed in claim 43 wherein the therapeutic treatment is for use in the healing of wounds (acute and chronic), and the treatment of fibrotic disorders, ulcerative colitis, inflammatory bowel disease, epilepsy, cardiovascular reperfusion injury, cerebral reperfusion injury, hypertension, cystic fibrosis, psoriasis, para-psoriasis, peptic ulcers, gastric ulcers, duodenal ulcers, diabetic ulcers, dementia, oncology and AIDS.

46. (Currently Amended) The conjugate according to claim 29 wherein R_1 , R_2 , R_3 and R_4 is a ~~are independently hydrogen,~~ substituted or unsubstituted C_{1-4} alkyl, aryl, halide, amine, alkoxy, ether, ester, alcohol, phenol, nitro, amide, thiol, sulphate, phosphate, or phosphonate.

47. (Previously Presented) The conjugate according to claim 30 wherein Z_1 , Z_2 , Z_3 and Z_4 are independently hydrogen, substituted or unsubstituted C_{1-4} alkyl, aryl, halide, amine, alkoxy, ether, ester, alcohol, phenol, nitro, amide, thiol, sulphate, phosphate, or phosphonate.

48. (Previously Presented) The conjugate according to claim 37 wherein the anti-infective agent is an antibiotic or antiviral agent.

49. (Previously Presented) The method according to claim 42 wherein said other arthritic condition is oosteoarthritis.

50. (Previously Presented) The method according to claim 44 wherein said gastrointestinal disorder is Crohn's disease.